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EXAMINER	
JAISLE, CECILIA M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,971	YOSHIKAWA ET AL.	
	Examiner	Art Unit	
	CECILIA M. JAISLE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 14-33* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14-19 and 24-33* is/are rejected.

7)☒ Claim(s) *20-23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01-14-2005 & 12-03-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Election/Restrictions

Applicant's election of Group II in the Response filed April 4, 2008, to the Restriction mailed Mar. 4, 2008, is acknowledged. Since no traverse is mentioned, the election is without traverse. Applicant should delete non-elected subject matter from the claims in response to this action.

Claims 1-11 and 14-33 are under examination, only to the extent that they are directed to elected subject matter. Claim 12 is withdrawn from examination as directed to non-elected subject matter.

Claim Rejections. 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 32 and 33 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections. 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of non insulin-dependent diabetes mellitus (NIDDM, or Type 2 diabetes), does not reasonably provide enablement for treatment or prevention of all diseases for which dipeptidyl peptidase IV inhibition is effective. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 28 and 29, whether drawn to a compound or a composition, are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. An agent that inhibits dipeptidyl peptidase IV is effective only for treatment, not prevention, of type 2 diabetes mellitus. All other therapeutic or preventative intended uses recited in claims 28 and 29 are not enabled by the disclosure.

Factors considered in determining whether claimed inventions are enabled by the disclosure are –

(A) The breadth of the claim;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) Claims 28-33 are of indeterminate scope, as explained in the rejection of those claims under 35 U.S.C. 112, second paragraph. Some of the subject matter within the scope of the claims is, however, ascertainable. One disease for which inhibition of dipeptidyl peptidase IV is an effective treatment is NIDDM.

(B) The nature of the invention in claims 28-33 is medical treatment and therapeutic or preventative agents.

(C) As evidence for the state of the art at the time the invention was made, with respect to therapeutic application of inhibitors of dipeptidyl peptidase IV, the examiner directs applicants to the following four references:

Reimer et al, Europ. J. Endocrinol., vol. 146, pages 717-727 (2002).

Ahren et al, Diabetes Care, vol. 25(5), pages 869-875 (2002).

Sudre et al, Diabetes, vol. 51, pages 1461-1469 (2002).

Evans, M., Investigational Drugs Journal, vol. 5(6), pages 577- 585 (June 2002).

Reimer report experiments showing that the dipeptidyl peptidase IV inhibitor "NVP DPP728" in mice over 4- and 8-week periods improved glucose tolerance, increased insulin levels, improved islet function in the pancreas (pp. 723-724), and conclude (p. 725) that the compound is a potential therapeutic agent for type 2 diabetes.

Ahren report that the compound "NVP DPP728," a dipeptidyl peptidase IV inhibitor, is a feasible treatment for type 2 diabetes in humans (p. 872).

Sudre report that in obese rats, the dipeptidyl peptidase IV inhibitor "FE 999011" delays occurrence of diabetes and improves glucose tolerance (p. 1467).

Evans is a patent literature review circa 2002, and describes the 2002 state of the art. The only feasible therapeutic application for dipeptidyl peptidase IV inhibitors is in type 2 diabetes treatment. P. 578 states, "The initial interest in DPP-IV inhibitors and their possible role in immunology has not been pursued due to a lack of positive results." P. 583 states that DPP-IV inhibitors are promising type 2 diabetes treatment agents. Although more therapeutic applications for DPP-IV inhibitors could be discovered, Evans concludes, "there is a large scope for future developments."

(D) The person of ordinary skill with respect to method claim 31 is a physician, since the claim is drawn to a medical treatment method.

(E) The level of predictability in the art is quite high with respect to the treatment of type 2 diabetes, i.e., type 2 diabetes is likely to be effectively treated by administering a compound according to the invention. On the other hand, the level of predictability for all other diseases is quite low. One of ordinary skill in the art would not be able to predict in advance how a given disease (other than type 2 diabetes) would be affected by a compound according to the invention - this must be empirically determined.

(F) The specification does not provide any direction other than some experiments which demonstrate the same types of effects as shown in Reimer and Sudre. The last page of the specification alleges that the compounds according to the invention are useful as treatments for a host of diseases and conditions not related to the therapeutic

activity demonstrated for the compounds. The specification offers no suggested dosage range or correlation with specific diseases treated.

(G) The working examples in the specification demonstrate the effect that compounds of the invention have on glucose tolerance in rats, including obese rats, and *in vitro* enzyme inhibition data for selected compounds.

(H) For one of ordinary skill in the art to realize the full scope of claims 28-33, programs in many unrelated medical sub-disciplines would have to be undertaken. The preponderance of evidence, relating to what is known about compounds having the same pharmacological properties as those instantly claimed, suggests that type 2 diabetes mellitus treatment was the only feasible therapeutic application for such compounds in 2002, when the invention was made. To expand the scope of diseases treated with a compound according to the invention beyond treatment of type 2 diabetes mellitus would require an undue amount of experimentation given the guidance provided in the disclosure and what was known at the time the invention was made.

Claims 1-11 and 14-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Formula I compounds and their salts, does not reasonably provide enablement for their hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The following reasons apply to this rejection.

The claims, in embracing hydrates, are not enabled. The specification prophesizes hydrates, but the numerous examples presented all failed to produce a hydrate. The evidence of the specification is clear: These compounds do not possess the property of forming hydrates; there is no evidence that such hydrates even exist.

Applicants' attention is drawn to Revised Interim Utility and Written Description Guidelines, 66 FR 1092-1099 (2001), emphasizing that "a claimed invention must have a specific and substantial utility." MPEP 2163, *et. seq*. This application's disclosure is insufficient to enable the instantly claimed hydrates based solely on the disclosure of the compounds and salts, absent the disclosure of a valid method of preparing the hydrates. The state of the art indicates the requirement for undue experimentation.

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior art; (4) the level of predictability in the art; (5) the amount of direction provided by the inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make the invention based on the content of the disclosure. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also *In re Goodman* 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

(1) Breadth of claims.

(a) Scope of the hydrates. The claims cover potentially millions of hydrates of the claimed substituted imidazopyridazine compounds.

(b) Scope of the methods of preparing the hydrates. The scope of methods is stated above, as well as the fact that the specification contains not one disclosure of the preparation of a hydrate of the claimed compounds.

(2) The nature of the invention and predictability in the art: Preparation of hydrates of the claimed compounds. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and preparation of hydrates are generally considered to be unpredictable. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). In the instant case, the preparation of hydrates is not sufficiently addressed by the instant disclosure.

(3) Direction or Guidance: That provided is very limited. Not a single hydrate is prepared in the specification. There is no specific disclosure of the specific conditions that will prepare and isolate the claimed hydrates.

(4) State of the Prior Art: Formation of hydrates is highly compound-specific in organic chemistry. Brittain, Chapter V of Polymorphism in Pharmaceutical Solids, 1999, pages 126-127, catalogs various difficulties of forming, isolating and identifying hydrates:

> Substances may hydrate/dehydrate in response to changes in environmental conditions, processing or over time if in a metastable thermodynamic state.

> It may not be practical or possible to maintain the same hydrate isolated at the discovery bench scale synthesis during scale-up activities for a hydrated compound. The choice of counterions to produce a more soluble salt form may also be dictated by the extent and type of hydration observed for a given salt and/or by the moisture level that may be safely accommodated by the dosage form.
>
> The physicochemical stability of the compound may raise issues during preformulation. Some hydrated compounds may convert to an amorphous form upon dehydration and some may become chemically labile. This Is true of cephradine dehydrate that dehydrates to become amorphous and undergoes subsequent oxidation. Other compounds may convert from a lower to a higher state of hydration yielding forms with lower solubility. In any case, the resulting "new" forms would represent unique entities that, depending on the dosage form, might have to be maintained throughout the manufacturing process and in the clinic and would impact on the regulatory status of the compound. Most often this demands that the form (usually crystalline) be identified and characterized with respect to handling conditions during the early pre-IND state of the development process.
>
> As dosage form development proceeds, changes in hydration state can result in variable potencies depending on handling conditions during weighing steps, the kinetics of the hydration/dehydration process, and the environmental conditions during processing. Differences in powder flow can result from changes in crystal form and/or morphology that may accompany the hydration/dehydration process. This can affect content uniformity in solid processing either in the mixing process or during transfer to other processing equipment such as tablet presses. …
>
> During and after manufacturing, moisture from the environment or that sealed in the package may redistribute throughout the dosage form and change the hydration state(s). These changes can, in turn, visit the negative consequences discussed above for the bulk drug on the dosage form. These can be manifest as changes in tablet/capsule dissolution rates (and perhaps bioavailability), changes in lyophile reconstitution times, tablet capping, chemical instability, discoloration and more. …

The present specification confirms Brittain. The specification fails to report making, isolating and/or identifying even one hydrate. Applicants must show making and identifying hydrates or cancel them from the claims.

(5) Working Examples: The specification prophesizes preparing hydrates of all of the claimed compounds, but no working examples or correlative prior art teachings actually show how to make and identify even a single hydrate.

Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present,

> "The first paragraph of 35 U.S.C. 112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."

Plant Genetic Syst. v. DeKalb Genet., 65 USPQ2d 1452, 1456 (Fed. Cir. 2003). "[T]he scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

(6) Skill of those in the art: See the discussion of Brittain above. The state of the art supports that to successfully prepare, isolate and identify a hydrate requires specific individualized methods.

(7) The quantity of experimentation needed: Based on the disclosure content, to make the invention would place an undue burden on one skilled in the pharmaceutical arts, since the disclosure gives the skilled artisan inadequate guidance regarding the method of making, isolating and identifying hydrates, for the reasons stated above.

Discussion of the above factors demonstrates that the present application sufficiently lacks enablement of the present claims. In view of the breath of the claims, the unpredictability of methods of making, isolating and identifying hydrates, one of

ordinary skill in this art would have to undergo an undue amount of experimentation to make the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states,

> A conclusion of lack of enablement means that, based on the evidence regarding each of the above [Wand] factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed.Cir. 1993).

This is a circumstance where the "specification is evidence of its own inadequacy" (*In re Rainer*, 153 USPQ 802, 807). Hydrates cannot be simply willed into existence. *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 states:

> The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist ... the examples of the '881 patent do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The same circumstance appears true here: no evidence shows that hydrates of these compounds actually exist; if they did, they would have formed. Applicants must show making hydrates or limit the claims accordingly.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 14-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the definition "A^0 represents a single bond" followed by the definition "A^1 represents a single bond" represents an impossible situation. It is not possible for a chemical compound to have two adjacent single bonds with no substituent intervening.

Claims 25, 26 and 28-30 are indefinite because it is not clear whether they are drawn to compounds or compositions. Claims 25, 26 and 28-30 each constitute a duplicate claim. If claims 25, 26 and 28-30 are intended to be compound claims, each is a substantial duplicate of claim 1; if they are intended to be composition claims, each is a substantial duplicate of claim 27.

Claim 31, in addition to being rejected for indefiniteness because it depends from an indefinite base claim, is indefinite because the full scope of the group consisting of "diseases for which the inhibition of dipeptidyl peptidase IV is effective" is unknown. The disease recited in claim 31 is limited to only those diseases for which inhibition of dipeptidyl peptidase IV is effective.

Claim 31 does not require that the compounds according to the invention be the agent which inhibits dipeptidyl peptidase IV to render a disease treatment included in the claim scope. Some dipeptidyl peptidase IV inhibitors which are different from those according to claim 1 could be the enzyme inhibiting agent and constitute the effective disease treatment. The level of inhibition is not defined, so the diseases are not fully defined. Different inhibition levels will afford different disease treatments.

That one of ordinary skill in the art would be able to identify one disease for which dipeptidyl peptidase IV inhibition constitutes an effective treatment does not rebut

the finding that all diseases characterized thusly would not be discernable to one of ordinary skill in the art. One such disease is non insulin-dependent diabetes mellitus.

Claims 32 and 33 recite the use of a compound of claim 1, but, since the claims do not set forth steps involved in the intended method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites use without active, positive steps defining how this use is practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-11, 14-24, 27 and 31-33 are rejected under 35 U.S.C. 102(a) as anticipated by US Pat. 7,109,192 (Hauel et al), based on the filing dates of provisional applications 60/437,438 (30 Dec. 2002) and 60/456,598 (21 Mar. 2003), both of which were filed before the U.S. filing date of the instant application. The earlier filed provisional application discloses all presently claimed compounds, and the later filed provisional application discloses compounds as well as method of treatment and pharmaceutical compositions comprising the compounds.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a certified translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Hauel discloses many compounds with an imidazo[4,5-d]pyridazine-4-one nucleus, as those according to the instant claims, where Z^1 is $C(R^2)$ and Z^2 is nitrogen.

A selection from Hauel's examples is described here (for each following Hauel example, R^2 is hydrogen, Z^2 is nitrogen and Z^1 is $C(R^2)$).

Hauel, Example 1, is a compound according to at least present claims 1-4, 6-8 (phenyl group substituent in X is optional), at least claims 9, 11, 14-16 (C is optional) and at least claims 19-23 where R1 is naphthalene-1-methyl (in claim 1, A° and A^1 are bonds and A^2 is benzyl (an aryl alkyl group); or in claim 14, A^{10} is alkylene, A^{11} is a bond, and A^{12} is aryl), X is phenyl, and T^1 is a 3-amino-piperid-1-yl group.

Hauel, Ex. 6, is a compound of present claims 1-4, 6-8 (claim 6, from which claim 8 depends, phenyl is optional), 9-11, 14-16 (C is optional) and 19-23 where R^1 is triazolo[4,3-a]pyridine-3-ylmethyl (claim 1, A° and A^1 are bonds, A2 is a 9-membered heteroaryl alkyl group; or claim 14, A^{10} is alkylene, A^{11} is a bond, and A^{12} is a 9-membered heteroaryl group), X is 2-butyn-1-yl (an alkynyl group), and T^1 is 3-amino-piperid-1-yl.

Hauel, Example 7, is a compound of present claims 1-4, 6-8 (claim 6, from which claim 8 depends, phenyl is optional), 9-11, 14-16 (C is optional) and 19-23 wherein R^1 is isoquinolin-1-ylmethyl (claim 1, A° and A^1 are bonds and A2 is a 10-membered heteroaryl alkyl group; or claim 14, A^{10} is alkylene, A^{11} is a bond, and A^{12} is a 10-membered heteroaryl group), X is 2-butyn-1-yl (an alkynyl group), and T^1 is 3-amino-piperid-1-yl.

Hauel, Example 90, is a compound of present claims 1-8 (the phenyl group substituent in X is optional), 9, 11, 14-16 (C is optional) and 19-23 wherein R^1 is benzyl

(in claim 1, A° and A^1 are bonds, A^2 is an aryl alkyl group; or in claim 14, A^{10} is alkylene, A^{11} is a bond, and A^{12} is aryl), X is benzyl (an aryl alkyl group), and T^1 is piperazine-1-yl.

Hauel, Example 96, is a compound according to present claims 1-3, 6-8 (phenyl in X is optional), 9, 11, 14-16 (C is optional) and 19-23 wherein R^1 is pyrid-2-ylmethyl (in claim, 1 A° and A^1 are bonds, A2 is a 6-membered heteroaryl alkyl group; or in claim 14, A^{10} is alkylene, A^{11} is a bond, and A^{12} is a 6-membered heteroaryl group), X is 3-methyl-2-buten-1-yl (C4 alkenyl group with one substituent), and T forms a 1,4-perhydro-diazepin-1-yl group (claims 2 and 3, one of m and n is 0 and the other is 1).

Hauel, Example 97, is a compound according to present claims 1-3, 6-8 (phenyl in X is optional), 9, 11, 14-16 (C is optional) and 19-23 wherein R^1 is isoquinolin-1-ylmethyl (in claim 1, A° and A^1 are bonds, A^2 is a 10-membered heteroaryl alkyl group; or in claim 14, A^{10} is a methylene group, A^{11} is a bond, and A^{12} is a 10-membered heteroaryl group), X is 3-methyl-2-buten-1-yl (a C4 alkenyl group with one substituent), and T^1 forms a 3-amino-piperid-1-yl group.

Hauel, Ex. 114, is a compound of claims 1-4, 6-8 (phenyl group in X is optional), 9-11, 14-16 (C, modified in claim 16, is optional) and 17-24 wherein R^1 is methyl (claim 1, A° and A^1 are bonds and A^2 is an alkyl group; or claim 14, A^{10} is a methylene group, A^{11} is a bond, and A^{12} is a hydrogen atom), X is 2-butyn-1-yl (an alkynyl group), and T^1 forms a 3-amino-piperid-1-yl group. This is the third named species in present claim 24.

Hauel, Example 125, is a compound of claims 1-3, 6-8 (optional substituent on the phenyl group in X), 9, 11, 14-16 (C is optional) and 19-23 wherein R^1 is benzyl (in claim 1, A° and A^1 are bonds, A2 is an aryl alkyl group; or in claim 14, A^{10} is alkylene,

A^{11} is a bond, and A^{12} is aryl), X is benzyl (an aryl alkyl group), and T^1 forms a 1,4-per-hydrodiazepin-1-yl group (claims 2 and 3, one of m and n is 0 and the other is 1).

Pharmaceutical compositions according to instant claim 27, comprising the active substances disclosed in Hauel and adjuvants useful for formulation, are found in Hauel, examples 224-231, pages 51 and 52.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauel. Hauel is applied to claims 17 and 18 as set forth in the rejection of claims 1-11, 13-24 and 27 under 35 U.S.C. 102(a). When the invention was made, compounds according to instant claims 17 and 18, R1 is cyanobenzyl would have been obvious to one of ordinary skill in the art given the teaching of Hauel.

Hauel discloses compounds wherein R3 is benzyl. Examples 90, 123 and 125 are some compounds according to present claim 1 where R1 is benzyl. Hauel expressly suggests a cyano group on R3 when R3 is phenyl alkyl (Hauel, ¶ [0019]).

One of ordinary skill in the art understands that teachings found in the general description of compounds in a given patent publication to be particularly applicable to preferred embodiments of the invention described therein. The difference between

compounds of present claims 17 and 18 and compounds of Hauel's examples 123 and 125 is the cyano group on the benzyl substituent. A cyano group is suggested by Hauel.

The motivation for one of ordinary skill in the art to make a compound according to Hauel where the R3 group of the compounds disclosed in Hauel (R1 in the instantly claimed compounds) is cyanobenzyl would have been to make inhibitors of dipeptidyl-peptidase IV, useful in treatment of obesity and NIDDM.

Claim 19 is rejected under 35 U.S.C. 103(a) as unpatentable over Hauel, applied against claim 19 in the rejection of claims 1-11 and 13-24 and 27 under 35 U.S.C. 102(a). When the invention was made, claim 19 compounds where R^2 is alkyl (A^{21} is a bond, and A^{22} is alkyl) would have been obvious to one of ordinary skill in the art.

Although all Hauel exemplified compounds have H at the position corresponding to R^2 in formula (I), instant claim 1, which renders claim 19 compounds anticipated by Hauel, the patent application publication expressly suggests an alkyl group at this position (¶ [0037]) and states that the alkyl group at R^4 is preferably methyl (¶ [0064]).

One of ordinary skill in the art, given the Hauel teaching, and motivated by a desire to make dipeptidyl peptidase IV inhibitors taught in Hauel, would find it obvious to make compounds according to the Hauel examples, and modify those compounds by including an alkyl group at R^4 in the compounds disclosed therein, which corresponds to the R^2 in the instantly claimed compounds. This modification is expressly suggested.

Claims 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauel. Although Hauel does not actually describe that a treatment method according to these claims was carried out, Hauel expressly suggests treatment of NIDDM and obesity with a compound disclosed therein. Page 11, in ¶ [0132], Hauel teaches that many other conditions are also treatable with Hauel compounds. Since treatment of only obesity and NIDDM are enabled by Hauel, claims 31-33 are rejected over Hauel insofar as the diseases embraced by the phrase "a disease in which the inhibition of dipeptidyl peptidase IV is effective" construe NIDDM and obesity.

The motivation for one of ordinary skill in the art to do so would have been to ameliorate the damaging effects of NIDDM and obesity in a patient, for which a dipeptidyl peptidase IV inhibitor is effective.

Claim Objections

In addition to being rejected under 35 U.S.C. 112, claims 1-3, 6, 7, 12, 14-15 and 19-22 are objectionable for placing claim phrases in parentheses. Parenthetical claim limitations render the claims indefinite, may be interpreted as implying there are other unspecified definitions for variables defined within the parenthetical phrases, and the parenthetical claim limitations are but one possible definition for variables thus defined.

In some claims, e.g., claims 14, 20 and 21, the majority of the claim is in parentheses. The presence of parenthetical claim limitations is awkward and inelegant.

Applicants should delete these parentheses from all claims except where required, such as partial structural formulae and claim status identifiers.

Claims Withdrawn from Examination

As noted in rejections under 35 U.S.C. 112, first and second paragraphs, claims 25, 26 and 28-30 have not been further examined on their merits. It is not possible to determine whether these claims are drawn to compounds or compositions.

Allowable Subject Matter

Claims 20-23, where R^2 is other than H, would be allowed if rewritten to overcome rejections under 35 U.S.C. 102, 112, 1st and 2nd paragraphs and include all limitations of the base claim and any intervening claims.

Hauel does not disclose compounds where the substituent corresponding to R^2 is other than hydrogen. No suggestion to include any substituent named in R^2 other than hydrogen is found in Hauel 's teaching relating to the R^4 position in compounds disclosed therein. In addition, claims 20-23 are patentable over all other prior art of record, whether taken individually or in any combination.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CECILIA M. JAISLE, J.D. whose telephone number is (571)272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624

CECILIA M. JAISLE, J.D.
7/1/2008